

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB2004/002657

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/569 C07K16/12 A61K47/48 C07H3/06 G01N33/563  
A61K39/112

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N A61K C07K C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, BIOSIS, Sequence Search

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>POLOTSKY VSEVOLOD Y ET AL: "Comparison of conjugates composed of lipopolysaccharide from Shigella flexneri type 2a detoxified by two methods and bound to tetanus toxoid"</p> <p>INFECTION AND IMMUNITY, vol. 62, no. 1, 1994, pages 210-214, XP002305348 ISSN: 0019-9567 the whole document</p> <p style="text-align: center;">----- -/--</p>	<p>1-3,5,8, 10-14, 16,17,24</p>



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

22 February 2005

Date of mailing of the international search report

22.03.05

Name and mailing address of the ISA

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PASSWELL JUSTEN H ET AL: "Safety and immunogenicity of improved Shigella O-specific polysaccharide-protein conjugate vaccines in adults in Israel" INFECTION AND IMMUNITY, vol. 69, no. 3, March 2001 (2001-03), pages 1351-1357, XP002305349 ISSN: 0019-9567 the whole document	1-3, 8-14,16, 17
X	PAVLIKOVA DANKA ET AL: "Treatment with succinic anhydride improves the immunogenicity of Shigella flexneri type 2a O-specific polysaccharide-protein conjugates in mice" INFECTION AND IMMUNITY, vol. 67, no. 10, October 1999 (1999-10), pages 5526-5529, XP002305350 ISSN: 0019-9567 the whole document	1,2,8, 10-14, 16,17,24
X	TAYLOR D N ET AL: "Synthesis, characterization and clinical evaluation of conjugate vaccines composed of the O-specific polysaccharides of shigella dysenteriae Type 1, Shigella flexneri type 2a and Shigella sonnei (Plesiomonas shigelloides) bound to bacterial toxoids" INFECTION AND IMMUNITY, AMERICAN SOCIETY OF MICROBIOLOGY, WASHINGTON, DC, US, vol. 61, no. 9, September 1993 (1993-09), pages 3678-3687, XP002144780 ISSN: 0019-9567 the whole document	1,2,8, 10-14, 16,17,24
X	CARLIN N I A ET AL: "MONO CLONAL ANTIBODIES SPECIFIC FOR O ANTIGENIC POLY SACCHARIDES OF SHIGELLA-FLEXNERI CLONES BINDING TO II II 3 4 AND 7 8 EPITOPES" JOURNAL OF CLINICAL MICROBIOLOGY, vol. 18, no. 5, 1983, pages 1183-1189, XP002305351 ISSN: 0095-1137 the whole document	24,34,35
X	MEI YUN: "Analysis of biological characteristics of monoclonal antibodies to Shigella flexneri 2a O-side chain of LPS" CHINESE JOURNAL OF MICROBIOLOGY AND IMMUNOLOGY (BEIJING), vol. 12, no. 5, 1992, pages 322-324, XP002305352 the whole document	24

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 99/03871 A (SCHNEERSON RACHEL ; POZSGAY VINCE (US); US HEALTH (US); ROBBINS JOHN B) 28 January 1999 (1999-01-28) the whole document	1-43
Y	POZSGAY VINCE ET AL: "Protein conjugates of synthetic saccharides elicit higher levels of serum IgG lipopolysaccharide antibodies in mice than do those of the O-specific polysaccharide from Shigella dysenteriae type 1" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 96, no. 9, 27 April 1999 (1999-04-27), pages 5194-5197, XP002305353 ISSN: 0027-8424 the whole document	1-43
Y	POZSGAY V.: "Synthesis of glycoconjugate vaccines against shigella dysenteriae type 1" JOURNAL OF ORGANIC CHEMISTRY, vol. 63, 1998, pages 5983-5999, XP002305374 the whole document	1-17
Y	WO 02/080964 A (BOUTONNIER ALAIN ; FOURNIER JEAN-MICHEL (FR); PASTEUR INSTITUT (FR)) 17 October 2002 (2002-10-17) the whole document	1-43
Y	CHU C ET AL: "Preparation, characterization, and immunogenicity of conjugates composed of the O-specific polysaccharide of shigella dysenteriae type 1 (shiga's bacillus) bound to tetanus toxoid" INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON, US, vol. 59, no. 12, 1 December 1991 (1991-12-01), pages 4450-4458, XP002079501 ISSN: 0019-9567 the whole document	1-43

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MULARD LAURENCE A ET AL: "Synthesis of the methyl glycosides of a di- and two trisaccharide fragments specific for the Shigella flexneri serotype 2a O-antigen" JOURNAL OF CARBOHYDRATE CHEMISTRY, vol. 19, no. 7, September 2000 (2000-09), pages 849-877, XP002305354 ISSN: 0732-8303 the whole document	1-17
Y	COSTACHEL CORINA ET AL: "Linear synthesis of the methyl glycosides of tetra- and pentasaccharide fragments specific for the Shigella flexneri serotype 2a O-antigen" JOURNAL OF CARBOHYDRATE CHEMISTRY, vol. 19, no. 9, December 2000 (2000-12), pages 1131-1150, XP002305355 ISSN: 0732-8303 the whole document	1-17
Y	SEGAT-DIOURY F ET AL: "Convergent synthesis of the methyl glycosides of a tetra- and a pentasaccharide fragment of the Shigella flexneri serotype 2a O-specific polysaccharide" TETRAHEDRON: ASYMMETRY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 13, no. 20, 18 October 2002 (2002-10-18), pages 2211-2222, XP004390581 ISSN: 0957-4166 the whole document	1-17
Y	BELOT F ET AL: "Synthesis of the methyl glycoside of a branched octasaccharide fragment specific for the Shigella flexneri serotype 2a O-antigen" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 43, no. 46, 11 November 2002 (2002-11-11), pages 8215-8218, XP004388411 ISSN: 0040-4039 the whole document	1-17
P,A	PHALIPON ARMELLE ET AL: "Shigellosis: innate mechanisms of inflammatory destruction of the intestinal epithelium, adaptive immune response, and vaccine development." CRITICAL REVIEWS IN IMMUNOLOGY. 2003, vol. 23, no. 5-6, 2003, pages 371-401, XP002305356 ISSN: 1040-8401 the whole document	

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>CLEMENT MARIE-JEANNE ET AL:            "Conformational studies of the O-specific Polysaccharide of Shigella flexneri 5a and of four related synthetic pentasaccharide fragments using NMR and molecular modeling."            JOURNAL OF BIOLOGICAL CHEMISTRY,            vol. 278, no. 48,            28 November 2003 (2003-11-28), pages            47928-47936, XP002305357            ISSN: 0021-9258            the whole document</p>	1-43
P,X	<p>BELOT FREDERIC ET AL: "Blockwise approach to fragments of the O-specific polysaccharide of Shigella flexneri serotype 2a: Convergent synthesis of a decasaccharide representative of a dimer of the branched repeating unit."            JOURNAL OF ORGANIC CHEMISTRY,            vol. 69, no. 4,            20 February 2004 (2004-02-20), pages            1060-1074, XP002305358            ISSN: 0022-3263            the whole document</p>	1-43
P,X	<p>WRIGHT KAREN ET AL: "Preparation of synthetic glycoconjugates as potential vaccines against Shigella flexneri serotype 2a disease."            ORGANIC &amp; BIOMOLECULAR CHEMISTRY. 21 MAY 2004,            vol. 2, no. 10, 21 May 2004 (2004-05-21),            pages 1518-1527, XP002305375            ISSN: 1477-0520            the whole document</p>	1-43
X	<p>WO 99/58679 A (GLAXO GROUP LIMITED;            BONNEFOY, JEAN-YVES, MARCEL, PAUL; CROWE,            SCOTT,) 18 November 1999 (1999-11-18)            sequences 11,12</p>	29, 30
A	<p>ISLAM M S ET AL: "Production and characterization of monoclonal antibodies with diagnostic potential against Shigella flexneri."            JOURNAL OF CLINICAL &amp; LABORATORY IMMUNOLOGY. AUG 1989,            vol. 29, no. 4, August 1989 (1989-08),            pages 199-206, XP009044302            ISSN: 0141-2760            the whole document</p>	

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HARTMAN A B ET AL: "Specificity of monoclonal antibodies elicited by mucosal infection of BALB/c mice with virulent <i>Shigella flexneri</i> 2a." CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY. SEP 1996, vol. 3, no. 5, September 1996 (1996-09), pages 584-589, XP002318615 ISSN: 1071-412X the whole document	
A	WO 99/32645 A (STINSON, JEFFREY, L; WONG, HING; O'BRIEN, ALISON, D; SCHMITT, CLARE, K) 1 July 1999 (1999-07-01) the whole document	
P,A	KIPRIYANOV SERGEY M ET AL: "Generation and production of engineered antibodies." MOLECULAR BIOTECHNOLOGY, vol. 26, no. 1, January 2004 (2004-01), pages 39-60, XP009044299 ISSN: 1073-6085 the whole document	
P,X	WO 03/100033 A (BIOGEN, INC; THE REGENTS OF THE UNIVERSITY OF CALIFORNIA; VIOLETTE, SH) 4 December 2003 (2003-12-04) sequence 2	29, 30
E	WO 2004/063335 A (APPLIED MOLECULAR EVOLUTION; WATKINS, JEFFRY, D; VASSEROT, ALAIN, P; M) 29 July 2004 (2004-07-29) sequence 77	29, 30

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Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing
    - ☒ contained in the international application as filed
    - ☒ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purpose of search
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
1-17, 24-35
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-17

Glycoconjugates comprising fragments of the O-specific antigen of Shigella Flexneri Type 2a and, their medical use.  
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Invention 2: Claims 18-23, 36-43

Polysaccharides consisting of fragments of the O-specific saccharides of Shigella Flexneri type 2a, and their use for the preparation of glycoconjugates.  
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Invention 3: Claims 24-35.

Antibodies, fragments thereof, and nucleic acids, vectors, host cells for the preparation thereof.  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9903871	A	28-01-1999	AU 8407298 A EP 1000076 A1 WO 9903871 A1	10-02-1999 17-05-2000 28-01-1999
WO 02080964	A	17-10-2002	EP 1372707 A1 WO 02080964 A1 US 2003068324 A1	02-01-2004 17-10-2002 10-04-2003
WO 9958679	A	18-11-1999	AU 763491 B2 AU 3836799 A BR 9910327 A CA 2328606 A1 CN 1308676 T EE 200000658 A EP 1076701 A1 WO 9958679 A1 HR 20000762 A1 HU 0102005 A2 ID 28088 A JP 2002514421 T NO 20005632 A NZ 507879 A PL 344019 A1 SK 16762000 A3 TR 200003281 T2 ZA 200006312 A	24-07-2003 29-11-1999 30-01-2001 18-11-1999 15-08-2001 15-04-2002 21-02-2001 18-11-1999 30-06-2001 28-10-2001 03-05-2001 21-05-2002 08-01-2001 27-02-2004 24-09-2001 10-07-2001 21-03-2001 23-12-2002
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WO 2004063335	A	29-07-2004	US 2004131613 A1 US 2004131612 A1 WO 2004063335 A2	08-07-2004 08-07-2004 29-07-2004